## II. Preliminary Remarks

Support for the amendments is found throughout the specification as filed. The amendments are believed to contain no new matter.

Support for new claim 110 is found on page 34, line 17, to page 35, line 3, of the specification.

New claim 111 is directed to subject matter indicated by the Examiner to be enabled (see pages 7-8 of the office action).

New claim 112 is directed to a method for treating hyperproliferative diseases and includes the limitations of claims 75 and 81 (allowed), the subject matter of which the Examiner has found to be enabled as amended.

New claim 113 directed to a method of inhibiting groups of epithelial carcinoma cells which includes the limitations of amended claim 75 and 83 (allowed), the subject matter of which the Examiner has found to be enabled.

## III. Informalities

### A. The Objections to the Claims Should Be Withdrawn

Claims 8 and 71 were objected to because of grammatical errors. The Applicants respectfully submit that the objections are moot in view of the foregoing amendments made in accordance with the Examiner's suggestions. In particular, in claim 8, the comma after "SEQ ID NO:5" has been deleted. Further, the word "an" has been inserted before the term "oligonucleotide" in claim 71.

Claim 85 has been objected to for the alleged recitation of an improper Markush group. The claim has been amended to recite a proper Markush group.

Claim 96 objected to as depending from a rejected base claim has been rewritten in independent form.

In view of the foregoing amendments, the Applicants request that the objections be withdrawn.

## IV. Patentability Arguments

### A. 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

In rejecting claims 2, 14-17, 19, 26, 29, 32, 75-79, 82, 88-89, 93, 95 and 97 as allegedly not enabled for several reasons including that the claimed invention was not supported by a sufficient written description and because as a result one skilled in the art would not know how to make and use the invention so that it would operate as intended (see Office Action at pages 7-8).

The Examiner noted on page 7 through page 8, first paragraph, that the following subject matter is enabled. (Pending claims containing all or part of this subject matter are indicated in parenthesis.)

1. A method of reducing photoaging in a mammal comprising topically administering to the epidermis of the mammal an effective amount of at least one oligonucleotide wherein said oligonucleotide is approximately 2-200 bases in length and wherein the oligonucleotide comprises a phosphodiester backbone, wherein the oligonucleotide comprises a nucleotide sequence consisting of a nucleotide sequence or a portion thereof of a sequence selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 8, 10, and 11. (Claims 1 and its dependents.)

2. A method of increasing melanin production in epidermal, comprising topically administering to said cells an effective amount of an oligonucleotide sequence, wherein the oligonucleotide sequence selected from the group consisting of pTpT,

SEQ ID NO: 1, 3, 5, and 11. (Claims 7 and its dependents; claim 14 and its dependents.)

3. A method of inhibiting the proliferation of skin cells comprising topically administering to said cells an effective amount of pTpT. (Claims 26 and its dependents; claims 100, 101 and 102 and their dependents.)

4. A method of inhibiting malignant skin cells in a mammal comprising topically administering to the skin cells an effective amount of a composition comprising at least one oligonucleotide comprising a phosphodiester backbone, wherein the oligonucleotide is selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 6, and pTpT. (Claims 88 and its dependents.)

5. A method of inhibiting malignant skin cells in a mammal, comprising directly administering to the cells an effective amount of DNA fragments that comprise a phosphodiester backbone and are about 2-200 nucleotides in length, the DNA fragments being selected from the group consisting of: single-stranded DNA fragments, deoxynucleotides, dinucleotides, dinucleotide dimers and combinations thereof. (Claims 88 and its dependents.)

6. A method of inhibiting malignant skin cells of a mammal, comprising topically administering to said cells an effective amount of pTpT. (Claims 88 and its dependents.)

7. A method of increasing melanin production in epidermal cells, wherein said method comprises topically administering to said cells an effective amount of a composition comprising at least one single-stranded oligonucleotide, wherein the oligonucleotide has a phosphodiester backbone, and wherein the oligonucleotide

comprises SEQ ID NO: 5 or is a functional fragment of SEQ ID NO: 5. (Claims 17 and its dependents; and claim14, and its dependents.)

With regard to the rejections regarding *inter alia* unpredictability of oligonucleotide therapy, the applicants reiterate and incorporate by reference their arguments with respect to enablement and written descriptive support set out in their response to the Office Action filed on 6 September 2002.

Nevertheless, in accordance with the Examiner's statement that certain subject matter is enabled for certain of the indicated oligonucleotides and methods of administration, the claims have been amended so as to recite the subject matter indicated by the Examiner to be allowable. This does not indicate acquiescence to the Examiner's position but rather is being done to expedite allowance of the claims. The applicants reserve the right to pursue subject matter deleted from the amended claims in a duly filed continuation application.

In view of the foregoing amendments, the applicants submit that the pending claims are in condition for allowance and early indication thereof is earnestly solicited.

The Examiner is invited to telephone the undersigned with any questions or suggestions which may help expedite allowance of the claims.

Respectfully submitted,

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